

**SYNTHESES OF REGIOSPECIFICALLY MESO FUNCTIONALIZED  
DIPYRROMETHANES, PORPHYRINS, AND DIPHENYLETHANE-  
LINKED BISPORPHYRINS<sup>§</sup>**

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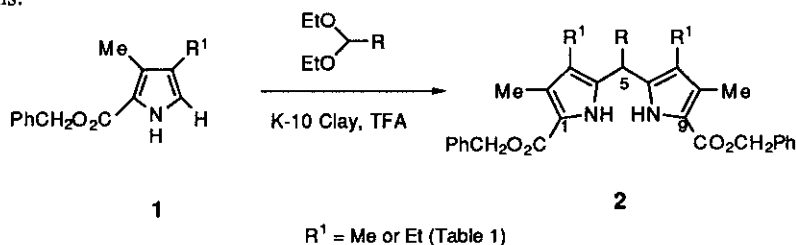
**Abstract** - Acid catalyzed condensation of 2-unsubstituted pyrroles with diethyl acetals permits preparation, in good yields, of a variety of meso-functionalized dipyrromethanes. Subsequent use in the so-called MacDonald "2+2" condensation provides 5-functionalized porphyrins and, eventually, benzochlorin derivatives. A novel application of a reductive coupling scheme, utilizing Ni(0), provides diphenylethane-linked bisporphyrins, which are potential models for electron transfer studies.

The synthesis, chemistry and spectroscopy of stilbene (1,2-diphenylethylene) meso-linked bisporphyrins have been reported.<sup>1</sup> So far as we are aware, the reduced variant, 1,2-diphenylethane linked bisporphyrins, have never been described in the literature. In principle, the ethylene tether of stilbene-linked dimeric porphyrins could be transformed into the corresponding ethane linkage by catalytic hydrogenation. Unfortunately, several problems may be encountered in hydrogenation of free base porphyrins, typical examples being low yields, sluggish reactions, and troublesome porphyrinogen formation. In this paper we report new porphyrin methodology for preparation of the more flexible 1,2-diphenylethane-linked bisporphyrins, the target compounds being obtained directly from appropriate monomeric free base or metalloporphyrin precursors, which were in turn prepared from dipyrromethanes using the MacDonald "2+2" approach.<sup>2</sup> The bisporphyrins are obtained by low valent nickel reduction. Transition metals in low valent oxidation states have recently been used as reagents for reductive homocoupling reaction of simple benzylic halides.<sup>3</sup> Though such reductive coupling reactions have been employed

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<sup>§</sup> Dedicated to Professor Rolf Huisgen, a frequent visitor to UC Davis, on the occasion of his 75th birthday.

extensively to dimerize a number of benzylic halides, this methodology has not previously been applied to any porphyrin systems.

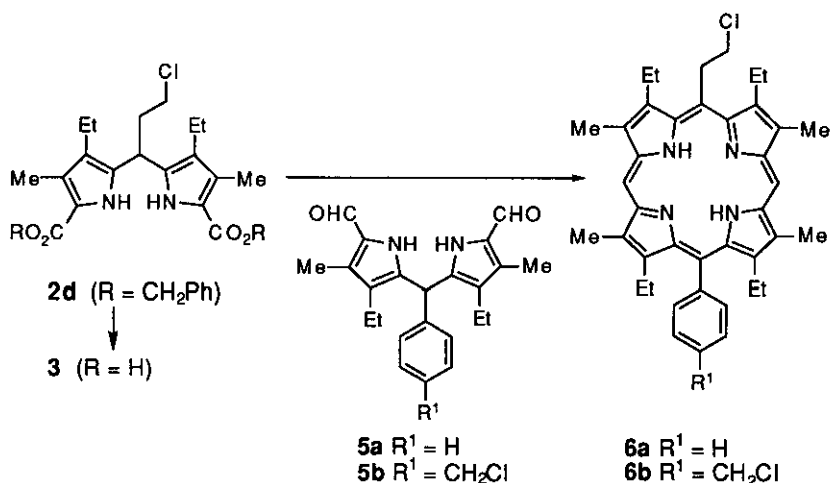


5-Chloromethyl-dipyrromethanes such as **2a** (Table 1) can be prepared in good yield (91%) *via* acid catalyzed condensation of 2-unsubstituted pyrroles (**1**) with chloroacetaldehyde diethyl acetal (Aldrich) using TFA-acidified Montmorillonite K-10 clay suspended in  $\text{CH}_2\text{Cl}_2$ .<sup>4</sup> We have extended the scope of this methodology [using dimethoxyacetals for compounds (**2b**) and (**2e**)], to the preparation of a variety of 5-functionalized dipyrromethanes (**2a-2e**) in good to excellent yields (62-91%) and with minimal or no chromatographic purification (Table 1).

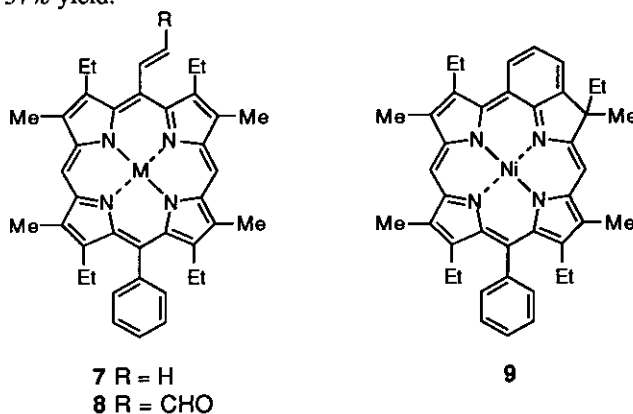
**Table 1:** Yields for Transformation **1**  $\rightarrow$  **2**

product	R	yield (%) <sup>a</sup>
<b>2a<sup>b</sup></b>	$\text{CH}_2\text{Cl}$	91
<b>2b<sup>c</sup></b>	$\text{CH}_2\text{CO}_2\text{Me}$	62
<b>2c<sup>c</sup></b>	$\text{CH}_2\text{CH}_2\text{OH}$	65
<b>2d<sup>c</sup></b>	$\text{CH}_2\text{CH}_2\text{Cl}$	87
<b>2e<sup>c</sup></b>	$\text{CO}_2\text{Me}$	64 <sup>d</sup>

<sup>a</sup>All structures were confirmed by elemental analysis, <sup>1</sup>H nmr, and HRms. <sup>b</sup>R<sup>1</sup> = Me. <sup>c</sup>R<sup>1</sup> = Et. <sup>d</sup>Prepared using pyridinium *p*-toluene sulfonate in toluene at 120°C.



The dipyrromethanes shown in Table 1 are useful intermediates for the synthesis of meso-substituted porphyrins. For example, condensation of the 5-chloroethyldipyrromethane-1,9-dicarboxylic acid (**3**) [obtained by catalytic hydrogenation of **2d** ( $R = \text{CH}_2\text{Ph}$ )] with 5-phenyl-1,9-diformyldipyrromethane (**5a**) under modified MacDonald conditions,<sup>2b</sup> gave the meso-chloroethylporphyrin (**6a**) in 28% yield. Condensation of **3** with the 5-(p-chloromethyl)phenyl derivative (**5b**) similarly gave the desired 5,15-substituted porphyrin (**6b**) in 27% yield. Reaction of **6a** with aqueous NaOH at 120°C yielded the desired meso-vinylporphyrin (**7**) ( $M = 2\text{H}$ ), in quantitative yield; the <sup>1</sup>H nmr spectrum showed two 1 proton vinyl doublets at 5.64 and 6.31 ppm and a 1 proton doublet of doublets at 9.35 ppm. After insertion of Ni(II) [by heating with nickel(II) acetoacetonate in *p*-xylene], treatment of **7** ( $M = \text{Ni}$ ) with the Vilsmeier reagent from POCl<sub>3</sub> and DMF<sup>5</sup> yielded the desired nickel(II) meso-acrolein porphyrin (**8**) in 57% yield.



Porphyrin (**8**) ( $M = \text{Ni}$ ) was cyclized to afford the corresponding nickel(II) benzochlorin (**9**) in 83% yield by stirring in conc. H<sub>2</sub>SO<sub>4</sub> at room temperature.<sup>6</sup> A pronounced red shift in the optical spectrum from 568 to 671 nm indicated the formation of the chlorin derivative. The <sup>1</sup>H nmr spectrum included two high-field meso-proton singlets (8.81 and 7.73 ppm) and four methyl singlets (3.03, 2.89, 2.80 and 1.85 ppm).

Porphyrin (**6b**) was found to be amenable to reductive coupling, as applied previously by Rieke and coworkers to much smaller systems.<sup>3a,b</sup> The nickel(II) complex of porphyrin (**6b**) was homo-coupled to afford a 51% yield of the corresponding 15,15'-bis(chloroethyl)-5,5'-diphenylethane linked bisporphyrin (**10**) by stirring with Ni(0) initially at room temperature and then heating at 70°C in dimethoxyethane (DME). The reagent was prepared *in situ* by reaction of nickel(II) iodide, naphthalene, and lithium metal in DME at room temperature. The presence of the ethane bridge was confirmed in the <sup>1</sup>H nmr spectrum by a resonance at 3.40 ppm. The visible absorption spectra of the monomeric porphyrin and the bis-porphyrin (Figure 1) are virtually identical. A major side product (38%) was the reduction product, 15-chloroethyl-5-tolylporphyrin (**11**).

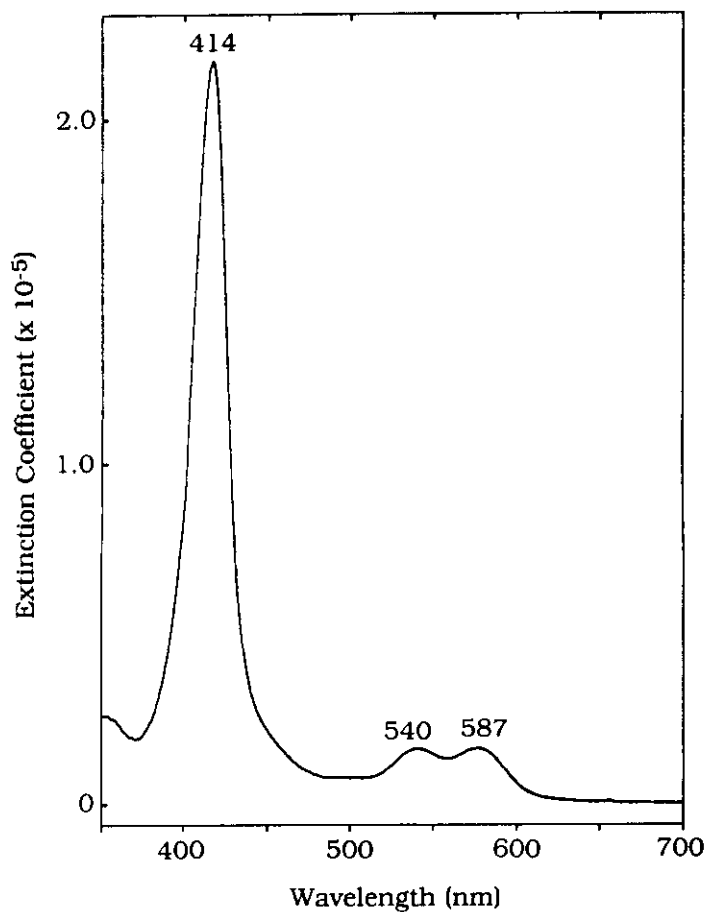
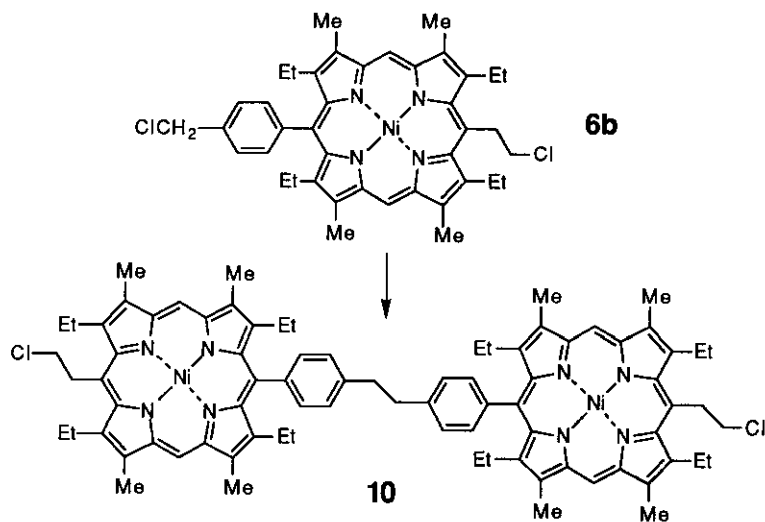
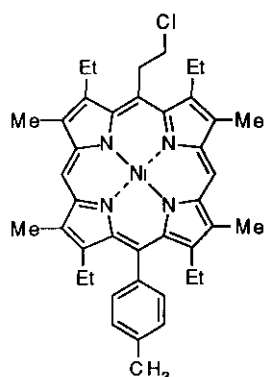


Figure 1: Optical Spectrum, in  $\text{CH}_2\text{Cl}_2$ , of Diphenylethane-linked Bisporphyrin (**10**).





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Other aspects of this methodology will be reported in due course.

#### ACKNOWLEDGMENTS

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